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A test for objective diagnosis of nasal hyperreactivity *

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SUMMARY

The aim of this study was to develop a method for the objective diagnosis of nasal hyperreactivity. The method should be standardized and simple enough to be used in clinical practice. In the study nasal challenge test with histamine was performed. Ten healthy volunteers and ten patients with a history of nasal hyperreactivity entered the trial. Recordings of nasal mucosa congestion were made with rhinostereometry. The results indicate that this method can indeed be used for the objective diagnosis of nasal hyperreactivity.

Key words: nasal hyperreactivity, methacholine, rhinostereometry

INTRODUCTION

Nasal secretion, sneezing and congestion are physiological reactions to different stimuli, such as cold or polluted air. A certain amount of people, with no known history of allergy, chronic infection or other defined diseases, demonstrate a higher reactivity of the nasal mucosa and suffer from sneezing, nasal secretion or nasal blockage without known provoking stimuli. There is no sharp limit when these reactions are regarded as pathological; but when the nasal reactivity gives symptoms severe enough to make the individual suffer, it is regarded as pathological, and pharmacological treatment is given. The terms generally used for this condition - or disease - are nasal hyperreactivity or vasomotor rhinitis. In pneumology, clinical methods exist to verify bronchial hyperreactivity and to estimate the degree of bronchial responsiveness. The methods mostly used are challenge tests with histamine or methacholine. Registrations are made with spirometry were the fall in forced expiratory volume is registered according to Hargreave et al. (1982).

There is a great demand for a similar method for the objective diagnosis of hyperreactive rhinitis. Many attempts have been made to develop such a method. The main problem is the registration of the mucosal reaction. The method mostly used for this purpose is rhinomanometry (Ashan et al., 1958). However, although the mean values of the patient group differ significantly from the values of the healthy subjects, there is a considerable overlap, and there have been difficulties to find standardized procedures which are clinically useful (Broms, 1972; Borum, 1979; Wihl, 1983). According to a report by Borum (1979), in which registrations of secretion after methacholine challenge were made, this method seemed to fulfill the demands of a clinically useful method. This method has, however, not come to a common use. There now also exists acoustic rhinometry (Hillberg et al., 1989). This is a method to evaluate changes in the geometry of the nasal cavity, but it has not been used for diagnostic purposes in the case of nasal hyperreactivity.

In this study rhinostereometry is used for registration. Rhinostereometry is an optical measuring method with which nasal mucosa congestion can be registered with a high accuracy (Juto et al., 1982). It has previously been shown that it is possible to standardize nasal mucosal congestion in a histamine challenge test in healthy volunteers, with registration made by rhinostereometry (Hallén et al., 1992). No nasal mucosa congestion of >0.4 mm is measured when challenging with histamine concentration levels below 4 mg/ml. On the contrary, it is observed that there is a nasal congestion of >0.4 mm after challenging with higher concentrations of histamine (16 mg/ml) on the challenged side, and no swelling of 0.4 mm on the unchallenged side (Figure 1). However, the model used in these challenge tests is too time-consuming to be used for clinical purposes.

The aim of this study was to develop a method for the objective diagnosis of nasal hyperreactivity, and especially one that is possible to use in clinical practice. Therefore, this study was performed in two parts. Firstly, it was studied if it was possible to simplify the challenge test as used in our previous study (Hallén et al., 1992). Secondly, we used the simplified model to record the nasal mucosa reaction in healthy subjects and in patients with a history of nasal hyperreactivity. The rationale for the first part of the study is that it should be possible to challenge with only two concentrations of histamine; nasal mucosa congestion

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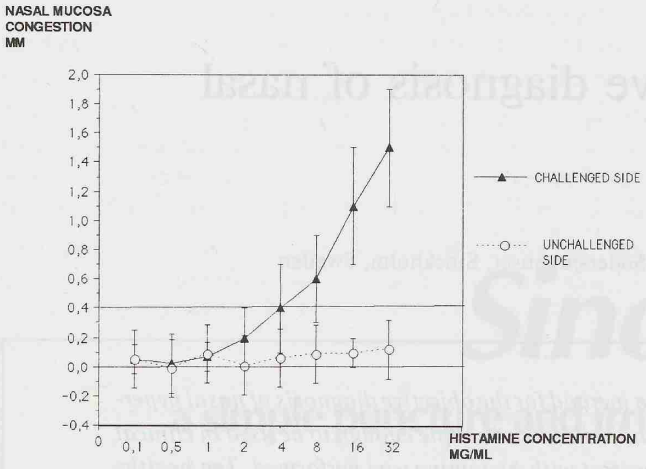

Figure 1. Mean values with error bars representing 95% confidence intervals for nasal mucosa congestion in healthy volunteers during histamine challenge with gradual raising of concentration levels of histamine. Recordings of congestion were made 5 min after challenge on the right side (challenged side) as well as on the left side (unchallenged side).

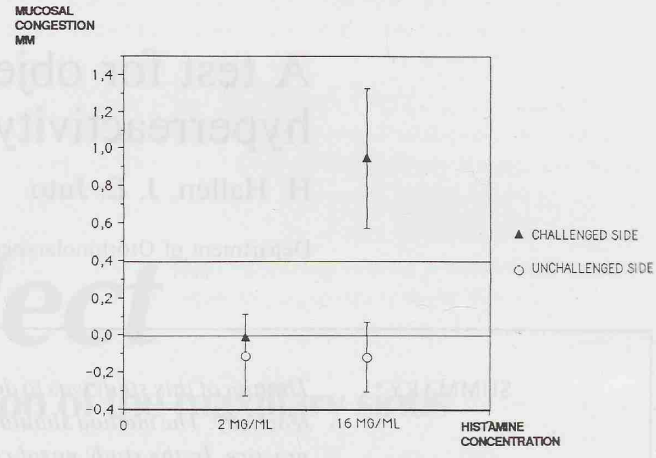

Figure 2. Mean values with error bars representing 95% confidence intervals for nasal mucosa congestion in healthy volunteers during histamine challenge with 2 and 16 mg/ml. Recordings of congestion were made 5 min after challenge on the right side (challenged side) as well as on the left side (unchallenged side).

of <0.4 mm will occur when challenging with low-doses of histamine (2 mg/ml) and, according to our previous study, congestion of >0.4 mm when challenging with 16 mg/ml. The hypothesis for the second part is that the patients with perennial rhinitis will have a more severe nasal congestion than the healthy group, when challenged with low doses of histamine (2 mg/ml), and that it will be possible to objectively distinguish between these two groups.

MATERIAL AND METHODS

Twenty persons entered the trial; 10 of them were healthy volunteers working at the clinic. All were women with ages ranging from 21 to 45 years. They had no history of rhinological disease and had not suffered from common cold or other airway diseases during the past two weeks. The remaining 10 persons were eight women and two men, with perennial rhinitis suffering from rhinorrhoea, sneezing or blockage. Perennial rhinitis in this respect was defined as having symptoms most days all over the year, and no symptom-free period for more than one week. No one in the group had a history of allergy, all subjects had negative skin-prick tests and normal levels of total IgE. Four patients had only blockage as a main symptom, two had rhinorrhoea, three had rhinorrhoea and blockage, and one patient had all three symptoms.

Histamine, in concentrations of 2 mg/ml and 16 mg/ml dissolved in saline and 0.5 % phenol, was used for challenging the nasal mucosa. The solution was syringed over the inferior turbinate on the right side. The position of the medial mucosal surface on the right and left inferior turbinate was recorded with rhinostereometry, before as well as 5 min after the challenge. Recordings were made on both sides of the nose, with the left side as control. The healthy volunteers were challenged with both histamine concentrations, i.e. 2 mg/ml and 16 mg/ml. The patients with perennial rhinitis were only challenged with 2 mg/ml.

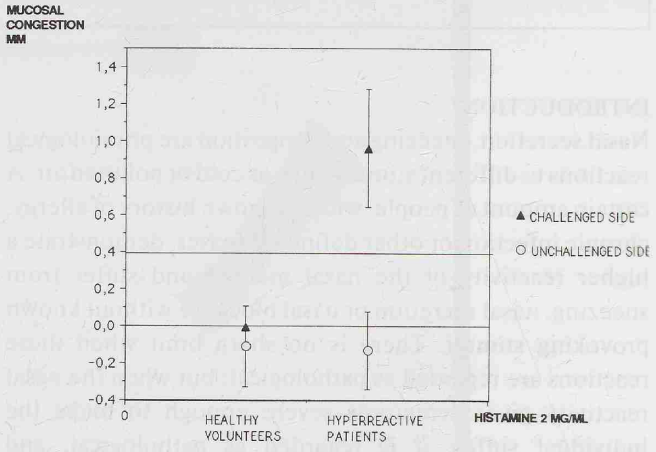

Figure 3. Mean values with error bars representing 95% confidence intervals for nasal mucosa congestion in healthy volunteers compared to patients with perennial rhinitis during challenge with histamine (2 mg/ml). Recordings of congestion were made 5 min after challenge on the right side (challenged side) as well as on the left side (unchallenged side). In the healthy group the mean congestion with 95% confidence interval is below the threshold value of 0.4 mm, and in the patient group the mean congestion with 95% confidence interval is more than the threshold value.

RESULTS

When challenged with 2 mg/ml the healthy volunteers had a nasal congestion below 0.4 mm, on the challenged side as well as on the unchallenged side. When challenged with 16 mg/ml, there was a congestion of 0.4 mm on the right side and less than 0.4 mm on the left side (Figure 2). This is in accordance with the previous study by Hallén et al. (1992).

In the second part of the study, in which patients with perennial rhinitis were compared to healthy volunteers, we found that the patients had a much more severe congestion than the healthy volunteers after being challenged with 2 mg/ml. The mean congestion with a 95% confidence interval in the patient group was >0.4 mm (Figure 3).

However, even each individual in the patient group had a congestion of 0.4 mm or more. In the healthy group no individual had a congestion of >0.3 mm. The registered congestion seemed to be independent of the type of main symptom. The group with blockage had a mean congestion of 0.9 mm, the group with rhinorrhoea had a mean congestion of 0.8 mm, and the group with both blockage and rhinorrhoea had a mean congestion of 0.7 mm. The only patient with all three symptoms had a congestion of 1.7 mm. It was also found that the congestion was ipsilateral.

DISCUSSION

In a previous study, Hallén et al. (1992) used nine different concentrations of histamine to provoke the nasal mucosa. The results could be dependent of a change in receptor sensibility during the challenge with the gradual raising of the concentrations; nevertheless, the results from the simplified challenge test indicate an equal reaction with only two concentrations used. This is in accordance with the first hypothesis in this study.

Our second hypothesis was that with only one crucial histamine concentration it should be possible to distinguish nasal mucosa reaction in healthy volunteers from that in patients with non-allergic perennial rhinitis. The hypothesis is based on the fact that hyperreactive patients have a higher reactivity to non-specific stimuli, compared to rhinologically healthy individuals, which is confirmed in this study. The results also indicate that it is possible to objectively distinguish between healthy individuals and patients with a history of nasal hyperreactivity.

Histamine was chosen in this study since it is a powerful provoking substance on the nasal mucosa (Doyle, 1990). In this study it was found that the histamine response is ipsilateral to the challenge, which supports the theory that histamine directly stimulates the H_1- and H_2-receptors on nasal blood vessels (Mygind et al., 1983).

With this challenge test two factors were expected to be crucial. The first was if it would be possible to get a response, in terms of congestion, in the patients that already had a swollen mucosa at the beginning. However, it showed that all individuals in the patient group had a reaction with more than 0.4 mm congestion. A possible reason for this is that the congestion had been present already during a long time, and is to a great deal due to an extravasal oedema and filled venous erectile tissue and since histamine is a potent vasodilatator, the immediate response cause further congestion by additional flow through the capillary network (Änggård, 1974). The second doubt was that individuals with enhanced secretion or sneezing as a main complaint, perhaps would respond with only increased secretion or sneezing. However, we found that the individuals with these symptoms also had a congestion of >0.4 mm.

This study indicates a high sensitivity and specificity. However, only a small number of subjects have been studied, and it is too early to discuss the method in these terms. This material is also highly dominated by women, especially in the healthy volunteer group, and since women have a higher nasal reactivity (Borum, 1979) this should not decrease the sensitivity of the method.

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